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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,500	11/13/2003	David F. Woodward	17605 (AP)	1201

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EXAMINER	
ANDERSON, REBECCA L	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 07/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/713,500	WOODWARD ET AL.	
	Examiner	Art Unit	
	Rebecca L. Anderson	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *9, 10, 16-18, 22, 23 and 30-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11-15,19-21 and 24-29* is/are rejected.

7)☒ Claim(s) *1-8,11-15,19-21 and 24-29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/29/05, 11/13/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

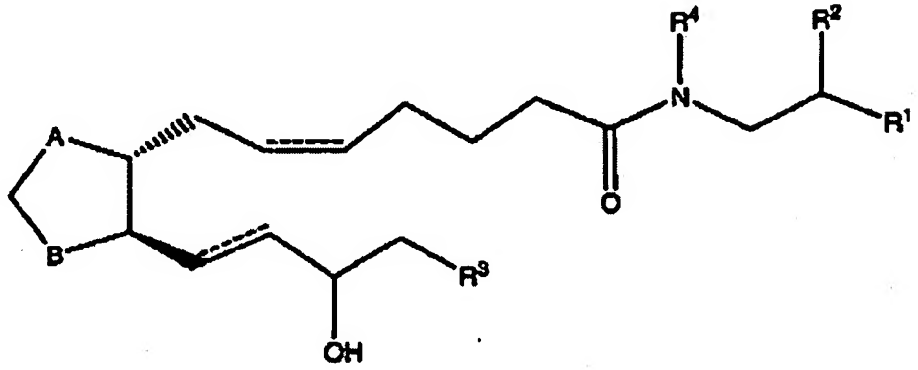
Claims 1-39 are currently pending in the instant application. Claims 1-8, 11-15, 19-21 and 24-29 are objected and rejected. Claims 9, 10, 16-18, 22, 23 and 30-39 are withdrawn from consideration as being for non-elected subject matter.

Election/Restrictions

Applicant's election with traverse of Group I and the further election of the compound 3 in the reply filed on 20 April 2006 is acknowledged. The traversal is on the ground(s) that there is no undue burden for search purposes. This is not found persuasive because the inventions are independent and distinct because there is no patentable co-action between the groups and a reference anticipating one member will not render another obvious. Each group is directed to art recognized divergent subject matter which require different searching strategies for each group. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner. However, upon reconsideration, the examiner will rejoin group II with group I. Claims 12-23 are hereby rejoined and claims 30-37 are NOT being rejoined. Because a claimed invention previously withdrawn from consideration under 37 CFR 1.142 has been rejoined, the restriction requirement between groups I and II as set forth in the Office action mailed 21 March 2006 on is hereby withdrawn.

Therefore, as stated on pages 3 and 4 of the restriction requirement, the election of group I (and rejoined group II) and the further election of the compound 3 in the reply filed on 20 April 2006 has resulted in the following elected invention:

The elected invention for search and examination is: the products (composition, compound and ophthalmic composition) of the formula



or a salt, ester, or prodrug thereof,

wherein:

A and **B** are as found in claim 12;

R1 is indolyl or monohydroxy or dihydroxy indolyl;

R2 is OH or H;

R3 is n-butyl, n-pentyl, or n-hexyl; cyclohexyl, Ar or W-Ar

Ar is phenyl or naphthyl optionally substituted with halogen, methyl or trifluoromethyl;

W is CH2

R4 is hydrogen, methyl, ethyl, iso-propyl, or n-propyl.

The remaining subject matter of claims 1-8, 11-15, 19-21 and 24-29 that is not drawn to the above elected invention and the subject matter of claims 9, 10, 16-18, 22, 23 and 30-39 stands withdrawn under 37 CFR 1.142(b) as being for non-elected subject matter. The remaining compounds which are not within the elected invention, which are independent and distinct from the elected invention and do not have unity with the

elected compound and therefore are withdrawn by means of a restriction requirement within the claims are, for example, the compounds of the formula the amine is selected from epinephrine, dopamine or diacetyl dopamine; wherein R1 is phenyl or monohydroxy or dihydroxy phenyl; Ar is thienyl, furanyl, or benzothienyl; W is N, S, or O, etc.

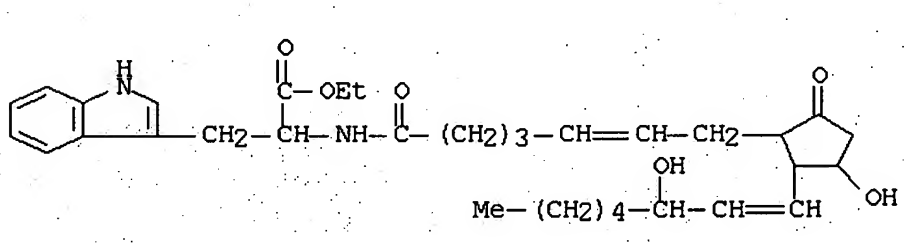
The above mentioned withdrawn compounds which are withdrawn from consideration as being for non-elected subject matter differ materially in structure and composition from the compounds of the elected invention. The withdrawn compounds differ from those of the elected invention by such as a thienyl, furanyl or benzothienyl, which are chemically recognized to differ in structure and function. This recognized chemical diversity of the compounds can be seen by the various classification of these compounds in the U.S. classification system, i.e. class 549 subclass 29(+) (thienyl), class 549 subclass 49(+) (benzothienyl), class 549 subclass 200(+) (furanyl), etc. Therefore, again, the compounds which are withdrawn from consideration as being for non-elected subject matter differ materially in structure and composition and have been restricted properly as a reference which anticipated but the elected subject matter would not even render obvious the non-elected subject matter. These withdrawn compounds are independent and distinct from the elected invention and do not have unity with the species elected and are therefore withdrawn by means of a restriction requirement within the claims.

The requirement is still deemed proper.

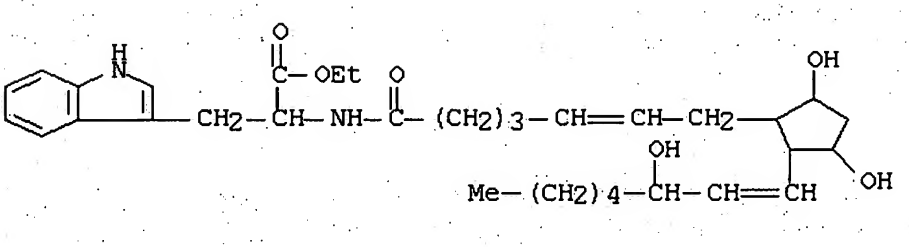
Claim Objections

Claims 1-8, 11-15, 19-21 and 24-29 are objected to as containing non-elected subject matter. Claims 1-8, 11-15, 19-21 and 24-29 presented drawn solely to the elected invention identified supra as **the elected invention for search and examination** would overcome this objection.

The closest prior art is JP 50013363 A2 which discloses compounds such as:



and



which differ from applicants instant elected invention by the C(=O)OEt group. The prior art reference neither anticipates or provided direction or motivation to arrive at applicants' instant elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-4, 12-15, 24-27 and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the elected invention wherein the prostaglandin is prostaglandin E, prostaglandin E2, prostaglandin F or prostaglandin F2a, or prostaglandin D2 and the amine is serotonin, does not reasonably provide enablement for analogs thereof The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

The nature of the invention is products of the elected invention wherein the prostaglandin can be an analog and serotonin can be an analog.

The state of the prior art

It is the state of the prior art that the term "analog" found in the claims is defined as compounds with similar electronic structures but different atoms (Hackh's chemical dictionary, 1972).

The predictability or lack thereof in the art

The predictability or lack thereof in the art is that analogs can have varying atoms.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the specification is found in the definitions of analog on pages 9-10 and 16-17, however, the definitions, include for example, wherein the cyclopentyl ring can contain heteroatoms and the 1-3 substituents (undefined or described) can be added to the aromatic ring. There are no working examples for analogs. There is no data present in the instant specification for the preparation of analogs. The generalized language for the definitionof analog, which includes any substituents on the aromatic ring and varying heteroatoms in the cyclopentyl ring does not suffice as it does not convey the detailed identity of the invention. The specification does not provide how to prepare the analogs.

The breadth of the claims

The breadth of the claims is the products of the elected invention wherein the prostaglandin can be an analog and serotonin can be an analog.

The quantity of experimentation needed

The quantity of experimentation is extremely high. One would need to modify atoms without enough direction from the instant specification as to how and to what atom, i.e. adding any substituent to the aromatic ring and how and which heteroatoms to the cyclopentyl ring.

The level of the skill in the art

The level of skill in the art is high. However, without a showing or guidance as to how to make varying analogs it would require undue experimentation to figure out what starting materials, solvents, temperatures and reaction times would provide other analogs.

This rejection could be overcome by amending the claim to delete the term "analog" from the claims.

Claims 12-15, 19 and 24-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the elected invention a salt or ester thereof does not reasonably provide enablement for any prodrug of the formula of the elected invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

The nature of the invention is the compounds of the formula of the elected

invention, its salts, esters and prodrugs.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that prodrugs can be formed by various mechanisms and vary depending on the functional groups present in the parent compound, i.e. different prodrugs would arise from parent compounds containing varying functional groups, such as a carboxylic acid, an alcohol or an amine, all of which would require differing mechanisms.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is for the compounds of the formula or the elected invention and pharmaceutically acceptable salts of the compounds and esters. There is no data present in the instant specification for the preparation of prodrugs of the instant compounds, except esters as defined on page 14. The definition of prodrug on page 14 only discloses esters. The generalized language for the definition of prodrug in the specification, besides the ester, does not suffice as it does not convey the detailed identity of the invention. In this case, the only generalized functional language only defines a function after a product has been prepared and does not provide enablement for the prodrug as the specification does not provide how to determine the prodrug and prepare the prodrug other than an ester.

The breadth of the claims

The instant breadth of the rejected claims is broader than the disclosure, specifically, the instant claims include any covalently bonded compound that would

release the active parent compound.

The quantity or experimentation needed and the level of skill in the art

While the level of the skill in the pharmaceutical arts is high, it would require undue experimentation of one of ordinary skill in the art to prepare any prodrug of the formula of the elected invention since prodrugs are formed by varying mechanisms and depend on the functional groups of the parent compound. The only guidance present in the instant specification is for the compounds of the formula of the elected invention, esters thereof and pharmaceutically acceptable salts thereof. There is no guidance or working examples present for any prodrug. Therefore, the claims lack enablement for prodrugs of the compounds. This rejection can be overcome by deleting the phrase "or prodrugs" from the instant claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim 1 includes the phrase "amide related to" which renders the claim indefinite. While the definition of "related to" can be found on page 16, the definition includes terms such as "derivative" which is defined as a compound, usually organic obtained from another compound by a simple chemical process or an organic compound containing a structural radical similar to that from which it is derived (Hackh's chemical dictionary, 1972). The phrase "related to" found in the claims renders the claims indefinite because it is unclear what compounds

are being claimed, i.e. what similar radical is found in the derivatives and encompassed by the instant claims. It is suggested that the claims be amended to the elected invention for search and examination to overcome this rejection and the phare "amide related to" be deleted from the claims.

Claims 12-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim 12 includes the phrase "monohydroxy or dihydroxy derivatives". The term "derivative" renders the claims indefinite as "derivative" which is defined as a compound, usually organic obtained from another compound by a simple chemical process or an organic compound containing a structural radical similar to that from which it is derived (Hackh's chemical dictionary, 1972). The term "derivative" found in the claims renders the claims indefinite because it is unclear what compounds are being claimed, i.e. what similar radical is found in the derivatives and encompassed by the instant claims. It is suggested that the claims be amended to the elected invention for search and examination to overcome this rejection and the term "derivative" be deleted from the claims.

Claims 5-8, 12-15, 19-21 and 24-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the claims contain the term "comprising" to describe the compound of the claims, for example:

"wherein the prostaglandin comprises" (claims 5-9);

"heteroatoms comprise S or O" (claim 7);

"a compound comprising" (claim 12);

"a compound of claim 12 comprising" (claims 20 and 21)

"said therapeutically active agent comprising" (claim 24).

The term comprising is considered open-ended language and therefore is including additional subject matter in the compounds described in the claims that is not described in the instant specification and is not particularly pointed out or distinctly claimed. A claim to a chemical compound cannot be open-ended, but must be claimed with precision. For example, heteroatoms comprise S or O, can be read to include additional atoms and groups other than S or O, however, the identity of the additional atoms or groups and how to determine the identity of the additional atoms or groups is not pointed out or distinctly claimed. This rejection can be overcome, for example, by deleting the open-ended language from the claim.

Claims 12-15, 19 and 24-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to

whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, the instant claims recite the broad recitation "prodrug" and the claim also recites "ester" which is the narrower statement of the range/limitation. Page 14 defines "prodrug" to include such as an "ester". It is unclear if the narrow feature of "ester" is exemplary or required.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

June 23, 2006

Rebecca Anderson
Patent Examiner
Art Unit 1626, Group 1620
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